



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
10/601,610	06/23/2003	Anke Klippel	1201.102	8727	
7590	02/28/2006		EXAMINER NGUYEN, QUANG		
Chiron Corporation Intellectual Property P.O. Box 8097 Emeryville, CA 94662-8097			ART UNIT		PAPER NUMBER
			1633		
DATE MAILED: 02/28/2006					

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/601,610

Applicant(s)

KLIPPEL ET AL.

Examiner

Quang Nguyen, Ph.D.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 10-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/23/03 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

Applicant's election without traverse of Group I (claims 1-9) in the reply filed on 12/05/05 is acknowledged.

Claims 10-21 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 1-9 are examined on the merits herein.

### ***Drawings***

The drawings are objected to because the schematic representations for "Myr•p110/ $\Delta$ kin", "Myr•p110\*/ $\Delta$ kin", "p110•H/ $\Delta$ kin" and "p110\*•H/ $\Delta$ kin" constructs are incomplete or not consistent for  $\Delta$ kin (lacking a X in a kinase box). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If

Art Unit: 1633

the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### ***Claim Objections***

Claims 8-9 are objected to because they encompass non-elected embodiments because a cell encompasses an *in vivo* cell in a treated patient or in a transgenic fly (see restriction dated 9/7/2005).

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8-9 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to a cell transformed with the polynucleotide sequences of the present invention. Since the polynucleotides of the present invention are intended to treat type II diabetes in humans (see at least page 14, lines 12-18), and the cell transformed with the polynucleotides is present or intended to be present in a human being treated for at least type II diabetes, said cell becoming integrated into the human being and therefore being an inseparable part of the human itself. The scope of the claim, therefore, encompasses a human being, which is non-statutory subject matter.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (Science 268:100-102, 1995) in view of Kapeller et al. (BioEssays 16:565-576, 1994), Varticovski et al. (Mol. Cell. Biol. 11:1107-1113, 1991) and Aronheim et al. (Cell 78:949-861, 1994).

Hu et al disclose the p110\* construct which comprises DNA encoding the p110 subunit of PI 3-kinase and the iSH2 portion of the p85 subunit that is attached to the NH2 terminus of p110 via a glycine-kinker (see Figure 1). The encoded protein is a constitutively active form of PI 3-kinase (see entire document). Hu et al further teach NIH 3T3 cells and *Xenopus laevis* oocytes recombinantly expressing p110\* that induces

Art Unit: 1633

transcription from the *fos* promoter and Ras-dependent oocyte maturation, respectively (see at least the abstract).

Hu et al do not teach specifically a construct further comprising a DNA encoding a membrane targeting sequence.

At the effective filing date of the present application, Kapeller et al already taught that localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation (at least page 571, columns 1 and 2; and Figure 4). Varticovski et al also taught that PI 3-kinase must be localized to a plasma membrane to work efficiently (see abstract and page 112, left hand column). Aronheim et al taught methods for localizing proteins to membranes by addition of amino acid sequences that contain signals for myristoylation, farnesylation, and palmitoylation (see the entire document).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time the invention was made to modify the p110\* construct of Hu et al by further adding DNA encoding membrane localization sequences in light of the teachings of Kapeller et al., Varticovski et al and Aronheim et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance the cellular responses or processes induced by PI 3-kinase because the localization of PI 3-kinase to the plasma membrane brings the enzyme into

Art Unit: 1633

closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation as taught by Kapeller et al and/or that PI 3-kinase must be localized to a plasma membrane to work efficiently as taught by Varticovski et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings Hu et al., Kapeller et al., Varticovski et al and Aronheim et al, coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

Claims 1, 4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klippel et al. (Mol. Cell. Biol. 14:2675-2685, 1994) in view of Kapeller et al. (BioEssays 16:565-576, 1994), Varticovski et al. (Mol. Cell. Biol. 11:1107-1113, 1991) and Aronheim et al. (Cell 78:949-861, 1994).

Klippel et al disclose constructs encoding the full-length p110 and p85 subunits of PI 3-kinase as well as their fragments, including the iSH2 portion of the p85 subunit (see Figure 1). Klippel et al further demonstrated that the complex containing either recombinant full length p85 or the iSH2-2 containing p85 fragments with the recombinant full length p110 exhibits PI 3-kinase activity in COS cells co-expressing

Art Unit: 1633

these recombinant constructs (page 2679, left hand column, last paragraph continues to first paragraph of right hand column and Figure 4).

Klippel et al do not teach specifically any recombinant construct comprising a DNA encoding a membrane targeting sequence.

At the effective filing date of the present application, Kapeller et al already taught that localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation (at least page 571, columns 1 and 2; and Figure 4). Varticovski et al also taught that PI 3-kinase must be localized to a plasma membrane to work efficiently (see abstract and page 112, left hand column). Aronheim et al taught methods for localizing proteins to membranes by addition of amino acid sequences that contain signals for myristoylation, farnesylation, and palmitoylation (see the entire document).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time the invention was made to modify the constructs of Klippel et al by further adding DNA encoding membrane localization sequences in light of the teachings of Kapeller et al., Varticovski et al and Aronheim et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance the cellular responses or processes induced by PI 3-kinase because the localization of PI 3-kinase to the plasma membrane brings the enzyme into



Art Unit: 1633

closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation as taught by Kapeller et al and/or that PI 3-kinase must be localized to a plasma membrane to work efficiently as taught by Varticovski et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings Klippel et al., Kapeller et al., Varticovski et al and Aronheim et al, coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

Claims 2-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klippel et al. (Mol. Cell. Biol. 14:2675-2685, 1994) in view of Kapeller et al. (BioEssays 16:565-576, 1994), Varticovski et al. (Mol. Cell. Biol. 11:1107-1113, 1991) and Aronheim et al. (Cell 78:949-861, 1994) as applied to claims 1, 4 and 8 above, and further in view of Eichner et al. (US 5,665,567).

The combined teachings of Klippel et al., Kapeller et al., Varticovski et al. and Aronheim et al. have been presented above. However, none of the references teaches that the nucleotide sequences encoding the p110 subunit of PI 3-kinase/its derivative or mutant and the p85 subunit of PI 3-kinase protein/its derivative or mutant are on the same construct.

However, at the effective filing date of the present application Eichner et al taught a bicistronic vector system in which an IRES sequence is located between the first and second cistrons for expression two different protein chains or different subunits of a protein such as a platelet derived growth factor (see at least the abstract). Eichner et al further disclose that bicistronic or multicistronic vectors were developed to avoid the problems connected with the stability of the mRNA of different transcripts, and that they can be used to achieve the synthesis of equimolar quantities of different protein chains or subunits (cols. 1-3).

It would have been obvious for an ordinary skilled artisan at the time the invention was made to modify to co-expressing the p110 subunit of PI 3-kinase/its derivative or mutant and the p85 subunit of PI 3-kinase protein/its derivative or mutant on a single bicistronic vector construct of Eichner et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to avoid the problems connected with the stability of the mRNA of different transcripts, and that they can be used to achieve the synthesis of equimolar quantities of the different protein chains, for this instance the catalytic p110 subunit and the regulatory p85 subunit of PI 3-kinase, as taught by Eichner et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings Klippel et al., Kapeller et al., Varticovski et al., Aronheim et al. and Eichner et al., coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,300,111 B1 in view of Kapeller et al. (BioEssays 16:565-576, 1994), Varticovski et al. (Mol. Cell. Biol. 11:1107-1113, 1991) and Aronheim et al. (Cell 78:949-861, 1994).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

U.S. Patent No. 6,300,111 B1 teaches the preparation of an expression vector comprising a DNA sequence encoding a constitutively active phosphatidylinositol 3-kinase polypeptide, wherein the polypeptide comprises a p85 subunit iSH2 domain

Art Unit: 1633

sequence or a conservatively modified variant thereof linked at the carboxy-terminus by a linker to the amino-terminus of a p110 subunit or a conservatively modified variant thereof and a cell containing the expression vector (see the entire document, especially claims 1-4)

However, the U.S. Patent No. 6,300,111 B1 does not teach that the expression vector further comprises a nucleotide sequence comprising a sequence encoding a cell membrane targeting sequence at the 5' end or 3' end of the DNA sequence encoding a constitutively active phosphatidylinositol 3-kinase polypeptide.

At the effective filing date of the present application, Kapeller et al already taught that localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation (at least page 571, columns 1 and 2; and Figure 4). Varticovski et al also taught that PI 3-kinase must be localized to a plasma membrane to work efficiently (see abstract and page 112, left hand column). Aronheim et al taught methods for localizing proteins to membranes by addition of amino acid sequences that contain signals for myristoylation, farnesylation, and palmitoylation (see the entire document).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time the invention was made to modify the expression vector construct of U.S. Patent No. 6,300,111 B1 by further adding DNA encoding membrane localization sequences to the

Art Unit: 1633

5' end or 3' end of the DNA sequence encoding a constitutively active phosphatidylinositol 3-kinase polypeptide in light of the teachings of Kapeller et al., Varticovski et al and Aronheim et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance the cellular responses or processes induced by PI 3-kinase because the localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation as taught by Kapeller et al and/or that PI 3-kinase must be localized to a plasma membrane to work efficiently as taught by Varticovski et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings U.S. Patent No. 6,300,111 B1, Kapeller et al., Varticovski et al and Aronheim et al, coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

Art Unit: 1633

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,300,111 B1 in view of Kapeller et al. (BioEssays 16:565-576, 1994), Varticovski et al. (Mol. Cell. Biol. 11:1107-1113, 1991) and Aronheim et al. (Cell 78:949-861, 1994).

The instant claims are directed to a polynucleotide sequence comprising: (a) a first nucleotide sequence comprising a sequence encoding the p110 subunit of PI 3-kinase protein or its derivative or mutant having a single or multiple nucleotide substitution, deletion or addition, and (b) a second nucleotide sequence comprising a sequence encoding a cell membrane targeting sequence, wherein said second nucleotide sequence being attached to the 5' or 3' end of said first nucleotide sequence; and a cell transformed with the polynucleotide sequence.

Claims 1-4 of U.S. Patent No. 6,300,111 B1 are drawn to an expression vector comprising a DNA sequence encoding a constitutively active phosphatidylinositol 3-kinase polypeptide, wherein the polypeptide comprises a p85 subunit iSH2 domain

sequence or a conservatively modified variant thereof linked at the carboxy-terminus by a linker to the amino-terminus of a p110 subunit or a conservatively modified variant thereof and a cell containing the expression vector.

The claims of the present application differ from the claims of the U.S. Patent No. 6,300,111 B1 in reciting that the polynucleotide sequence further comprises a nucleotide sequence comprising a sequence encoding a cell membrane targeting sequence.

At the effective filing date of the present application, Kapeller et al already taught that localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation (at least page 571, columns 1 and 2; and Figure 4). Varticovski et al also taught that PI 3-kinase must be localized to a plasma membrane to work efficiently (see abstract and page 112, left hand column). Aronheim et al taught methods for localizing proteins to membranes by addition of amino acid sequences that contain signals for myristoylation, farnesylation, and palmitoylation (see the entire document).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time the invention was made to modify the expression vector construct of U.S. Patent No. 6,300,111 B1 by further adding DNA encoding membrane localization sequences to the 5' end or 3' end of the DNA sequence encoding a constitutively active

Art Unit: 1633

phosphatidylinositol 3-kinase polypeptide in light of the teachings of Kapeller et al., Varticovski et al and Aronheim et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance the cellular responses or processes induced by PI 3-kinase because the localization of PI 3-kinase to the plasma membrane brings the enzyme into closer contact with its substrates, (e.g., phosphatidylinositol (4,5) bis-phosphate to generate phosphatidylinositol (3,4,5) triphosphate), and the lipid products of PI 3-kinase are essential for mediating various cellular effects such as cellular growth, transformation as well as cellular differentiation as taught by Kapeller et al and/or that PI 3-kinase must be localized to a plasma membrane to work efficiently as taught by Varticovski et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings U.S. Patent No. 6,300,111 B1, Kapeller et al., Varticovski et al and Aronheim et al, coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

### **Conclusion**

***No claims are allowed.***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, Celine Qian, Ph.D., may be reached at (571) 272-0777, or SPE, Dave Nguyen, at (571) 272-0731.

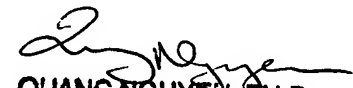


Art Unit: 1633

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.**

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

  
QUANG NGUYEN, PH.D  
PATENT EXAMINER